

CLAIMS

1. A reporter construct comprising:

an upstream region of a mammalian *CDK4* gene transcription start site comprising at least four c-MYC binding sites; and

5 a coding sequence for a reporter protein, wherein the upstream region is upstream of the coding sequence, and wherein the upstream region and coding sequence are operably linked so that a wild-type c-MYC upon binding to the upstream region activates transcription of the coding sequence.

10 2. The reporter construct of claim 1 wherein the c-MYC binding site is CACGTG.

3. The reporter construct of claim 1 wherein the region is at least 200 bp.

15 4. The reporter construct of claim 1 wherein the upstream region comprises a *CDK4* promoter.

5. The reporter construct of claim 1 wherein the mammalian *CDK4* gene is human *CDK4*.

20

6. A host cell comprising:

a reporter construct according to claim 1; and

a c-MYC protein;

wherein the c-MYC protein binds to the reporter construct and activates transcription of the coding sequence for the reporter protein.

7. The host cell of claim 6 which overexpresses c-MYC.

8. A method to screen test compounds for anti-cancer activity, comprising the steps of:

contacting a c-MYC protein with a reporter construct according to claim 1 in the presence of a test compound; and

monitoring expression of the reporter protein;

wherein a test compound which decreases expression of the reporter protein is a candidate anti-cancer agent.

9. The method of claim 8 wherein the reporter construct and the c-MYC protein are in a host cell and the test compound is contacted with the host cell.

10. The method of claim 8 wherein the reporter construct and the c-MYC protein are contacted in a cell-free transcription/translation system.

contacting tumor cells which comprise a genetic alteration which causes c-MYC overexpression with an agent which inhibits CDK4 enzymatic activity, whereby tumor cell growth is inhibited.

16. The method of claim 15 wherein the tumor cells are Burkitt's Lymphoma cells.

5

17. The method of claim 15 wherein the tumor cells are neuroblastoma cells.

18. The method of claim 15 wherein the tumor cells are colon cancer cells.

19. The method of claim 15 wherein the tumor cells have a t8;14 translocation.

20. The method of claim 15 wherein the tumor cells have a genetic amplification of *c-MYC*.

10

21. The method of claim 15 wherein the tumor cells have a mutation in *APC*.

22. The method of claim 21 wherein the tumor cells have a truncating mutation in *APC*.

23. The method of claim 15 wherein the agent is p16.

24. The method of claim 15 wherein the agent is a polypeptide comprising a truncated version of p16.

Sub B1
5 25. A method of screening compounds to identify those which have anti-cancer activity, comprising the step of:

contacting a cell which has a genetic alteration which dysregulates *c-MYC* expression with a test compound;

measuring activity of CDK4 in the cell, wherein a test compound which inhibits activity of CDK4 is identified as a candidate agent with anti-cancer activity.

26. The method of claim 25 wherein the cell is a Burkitt's Lymphoma cell.

10 27. The method of claim 25 wherein the cell is a neuroblastoma cell.

28. The method of claim 25 wherein the cell is a colon cancer cell.

29. The method of claim 25 wherein the cell has a t8;14 translocation.

30. The method of claim 25 wherein the cell has a genetic amplification of *c-MYC*.

31. The method of claim 25 wherein the cell has a mutation in *APC*.

Self
B27

32. The method of claim 21 wherein the cell has a truncating mutation in *APC*.

33. A method of determining responsiveness to an anti-cancer agent which inhibits CDK4 activity, comprising:

testing a cancer cell for the presence of a mutation selected from the group consisting of: a t8;14 translocation, an *APC* mutation, an amplification of *c-MYC*, and a β -catenin mutation;
wherein a cancer cell which is identified as having said mutation is identified as being susceptible to an inhibitor of CDK4.

34. The method of claim 33 further comprising the step of:

administering to the cancer cell an anti-cancer agent which inhibits CDK4 activity.